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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/227,518	01/08/99	TERRY	B 5441.200-US

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STEVE T ZELSON
NOVO NORDISK OF NORTH AMERICA INC
405 LEXINGTON AVENUE
SUIT 6400
NEW YORK NY 10174-6400

EXAMINER	
GABEL, G	
ART UNIT	**PAPER NUMBER**
1641	10

DATE MAILED: 04/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/227,518	TERRY ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-17* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4/5* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group 1, claims 1-16, with traverse, in Paper No. 9 filed 2/21/01 is acknowledged and has been entered. Claim 17 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being a claim drawn to a non-elected invention. Accordingly, currently, claims 1-16 are under examination.

Applicant's traversal regarding the restriction requirement set forth in Paper No. 6 is acknowledged. Applicant's argument, however, is not persuasive because restriction requirements are set forth for reasons of patentable distinction between each independent invention so as to warrant separate classification and search. The record set forth in the previous restriction requirement clearly indicated that the delineated inventions are in fact patentably distinct each from the other or independent from the other. The requirement is still deemed proper and is therefore made FINAL for reasons of record.

Priority

2. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application in the first sentence of the specification (37 CFR 1.78).

Drawings

3. This application has been filed with informal drawings which are acceptable for examination purposes only. However, formal drawings can be deferred until application is allowed by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 7-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 lacks antecedent support in reciting "the optical detector" and "the surface sample". See also claim 8.

Claim 10 is indefinite in reciting "capable exciting" because it fails to recite a positive limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. Claims 1-5, 9-10, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Sittampalam et al. (Current Opinion in Chemical Biology, 1997).

Sittampalam et al. teach cell based assay systems for use in high throughput screens wherein physiologically viable cells are coated onto a detector layer made from scintillant plastic so that upon contact with a test compound, the cells are monitored for bioactivity (cellular events, cytosolic calcium mobilization) (see page 365, column 1). The scintillant plastic is incorporated on 96 microwell plates wherein its surface is able to function as a pH sensing surface or a temperature sensing surface (see page 386, column 2). Sittampalam et al. also teach that illumination systems such as FRET systems are capable of exciting fluorescence of the detector layer and detecting changes in fluorescence or luminescence properties of the cells (see page 388, column 1). Sittampalam et al. teach that the most common method for detecting ligand interaction between test compounds (drugs) and targets in cells is to employ reporter genes.

6. Claims 1-2, 9-10, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Isacoff et al. (US 5,756,351).

Isacoff et al disclose a method for monitoring the physiological status of a cell. Specifically, Isacoff et al. disclose a method for screening test compounds for bioactivity (different cellular states, ligand binding, changes in distribution cross plasma membrane) using biomolecular optical sensors (see column 1, lines 35-58 and column 16-34). Isacoff et al. specifically disclose contacting an array of test compounds with a

detector layer comprising physiologically viable cells which produces a detectable response (different signals) which is indicative of bioactivity. The detectable response results from a change in fluorescence or luminescence property of the cells (see column 2). Detection is determined with an illumination system (luminescer generating system) which that is capable of exciting fluorescence or luminescence of the detector layer using selected wavelengths with defined order or time of duration (see column 1, lines 58-67 and column 3, lines 9-14).

7. Claims 1-2, 6-11, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Negulescu et al. (US 6,214,563).

Negulescu et al. disclose cell-based assays for use in drug discovery to screen large numbers of test compounds for bioactivity. Negulescu et al. specifically disclose contacting an array of test compounds with a detector layer that is comprised of physiologically viable cells (membrane compartments=cells) that are in physical and optical contact with a sensing surface (solid phase) (see column 3, lines 10-16 and column 5, lines 48-53). The viable cells on the detector layer preferably form a monolayer (single layer) (see column 14, lines 5-10). Negulescu et al. also disclose a sample distribution module wherein sample (test compound/chemical) from the sample surface (chemical well) is transported for contact with the cellular detector layer during the course of measurement (see column 17, lines 24-28). Alternatively, the cells from the detector layer can be contacted with the test compounds in chemical wells (see column 21, line 61 to column 22, line 8). The detection step uses different fluorescent

monitoring systems including those adapted to high throughput screening such multi-well platforms (see column 16, line 63 to column 17, line 3 and lines 44-47). If the test compound has bioactivity as a candidate modulator, there is a change in the fluorescence or luminescence property of the cellular detector layer which is determined by an illumination system by exciting the fluorescent reporter on the detector layer with various selected wavelengths (see columns 22 and 23).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 12-13 and 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sittampalam et al. (Current Opinion in Chemical Biology, 1997) or Negulescu et al. (US 6,214,563) in view of Chelsky et al. (US 5,856,083).

Sittampalam et al. and Negulescu et al. have been discussed supra. Sittampalam et al. and Negulescu et al. differ in failing to generate test compounds from a solid substrate or gel electrophoresis and exposing such array of compounds held on porous or non-porous substrate for contact with the detector layer.

Chelsky et al. disclose a lawn assay for screening and determining test compounds that are held on porous or non-porous solid support (see Abstract). Chelsky et al. specifically teach that the test compounds are linked to the support by a cleavable linker and upon cleavage of the linker, the test compounds diffuse into a support's vicinity comprising a colloidal matrix or a scintillant coated surface so that high concentrations of the test compounds are created on these supports (see column 3). Compounds released are then contacted with cellular receptors, i.e. membrane bound receptors on the scintillant supports so that binding interaction therebetween can be detected and measured using a fluorescence detection and illumination systems (see column 4). Chelsky et al. teach application of the invention in combinatorial libraries and drug discovery assays.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Chelsky in holding test compounds in solid support and diffusing them for contact with detector layers comprising cellular components such as taught by Sittampalam and Negulescu because Chelsky

specifically taught applicability of his teaching in high throughput drug discovery assays and Sittampalam and Negulescu specifically taught screening of an array of test compounds for bioactivity in cell based assays. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the teaching of Chelsky into the methods of Sittampalam and Negulescu because of the ease in simplifying the handling of arrays of multiple compounds incorporated into solid supports from steps such as weighing, transferring, and individual test compound distribution, thereby acquiring a rapid, large scale screening capability in high throughput screening methods (see column 1, Chelsky et al.).

9. No claims are allowed.

Remarks

10. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Zlokarnik et al. (US 6,200,762) disclose methods to identical chemicals with toxicological bioactivity.

Hamilton et al. (US 5,783,408) disclose method for screening potential obesity agents wherein cells (preadipocytes) are seeded into 96 well plates for testing of compounds (see column 10).

Burbaum et al. (US 5,876,946) disclose a high throughput method for screening test compounds (see columns 9 and 10).

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

4/12/01

Gailene R. Gabel
April 13, 2001

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
04/18/01